

Peng Liang  
Serial No.: 10/677,877  
Filed: October 2, 2003  
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**Amendments to the Drawings:**

Please replace Figures 1-5 of the subject application with the replacement sheets 1-5 attached as **Exhibit A.**

REMARKS

Claims 1-3 and 6-14 were pending in the subject application. Applicant has hereinabove amended claims 1-3, 6, 7 and 11-14 and added new claims 20-27. Accordingly, upon entry of this Amendment claims 1-3, 6-14 and 20-27 will be pending and under examination.

Applicant maintains that these amendments to the claims do not raise any issue of new matter, and that these claims are supported by the specification as originally filed.

Objection to the Drawings and Specification

In the December 4, 2006 Office Action the Examiner objected to the specification since it contains inconsistencies in Figure numbering versus the Drawings themselves.

In response, applicant has hereinabove amended the specification to correctly identify all Figures. Applicant maintains that these amendments to the specification do not raise any issue of new matter, and that these amendments are supported by the specification as originally filed. Accordingly, applicant respectfully requests the Examiner to remove this objection to the specification.

Further in the December 4, 2006 Office Action, the Examiner objected to Figure 4 since it was scanned too dark.

In response, applicant attaches replacement sheets 1-5 for all the Figures as **Exhibit A**.

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Applicants maintain that these replacement drawings do not contain any new matter, and that these replacement drawings are supported by the specification as originally filed.

Accordingly, applicant respectfully requests the Examiner to remove these objections to the drawings.

**Rejection Under 35 U.S.C. §103(a)**

In the December 4, 2006 Office Action, the Examiner rejected claims 1-3 under 35 U.S.C. §103(a) as allegedly obvious in view of Vuorio et al. (PCT International Publication No. WO 97/17988) and Burgeson et al. (U.S. Patent Publication No. 2003/0143564 A1). The Examiner alleged that Vuorio et al. disclose a fusion collagen using a method comprising a culturing host cells transformed with a recombinant DNA expression vector, and recovering the fusion protein from the cell culture. The Examiner also alleged that Burgeson et al. teach collagen XXII polypeptides linked to non-collagen polypeptides. The Examiner further alleged that it would have been obvious to a person skilled in the art to design a method for generating a secreted soluble trimeric fusion protein comprising collagen as disclosed by Vuorio et al. and to modify the invention by incorporating a non-collagen protein in a construct, as taught by Burgeson et al.

In response to the Examiner's rejection, applicant respectfully traverses on the ground that a prima facie case of obviousness cannot be established for the amended claims.

Under MPEP §2143, to establish a prima facie case of obviousness the cited references must teach or suggest every element of the claims.

Briefly, the pending claims recite a method for generating a disulfide bond-linked trimeric fusion protein, comprising: (a) creating a DNA construct comprising a transcriptional promoter linked to a template encoding a fused protein subunit comprising a signal peptide sequence followed by in-frame fusion to a non-collagenous polypeptide comprising a ligand binding domain which in turn is joined by in-frame fusion to a mammalian polypeptide which is heterologous from the non-collagenous polypeptide and which is capable of self-trimerizing said fused protein subunit to form said disulfide bond-linked trimeric fusion protein containing three ligand binding domains, wherein said trimeric fusion protein has an increased binding affinity to a ligand than a monomeric ligand binding domain (b) introducing said DNA construct into a eukaryotic cell; (c) growing said host cell in an appropriate growth medium under physiological conditions to allow said fused protein subunits to trimerize into the disulfide bond-linked trimeric fusion protein and to further allow the secretion of the trimeric fusion-protein and (d) isolating said secreted trimeric fusion protein from the culture medium of said host cell.

Vuorio et al. and Burgeson et al. do not disclose a method of generating disulfide bond-linked trimeric fusion proteins by trimerizing three fused protein subunits each containing a ligand binding domain. Neither cited reference discloses a portion of a fused protein subunit which is capable of self-trimerizing the entire fused protein subunit with two other fused protein subunits to form one disulfide bond-linked

trimeric fusion protein. Vuorio et al. only discloses fusion proteins containing different collagens. Burgeson et al. had a clear focus of patenting their newly identified collagen Type XXII and only discloses a generic approach for fusing collagen XXII with a non-collagen polypeptide with the purpose of either aiding its secretion/expression (e.g. by changing the signal peptide sequence) or aiding its purification and detection (e.g. by adding a GST tag or an Fc tag of IgG) (See paragraphs 148-149). In contrast, Burgeson et al. does not disclose or suggest a method of fusing collagen XXII to another polypeptide in such a manner as to allow its trimerization for increased biological activity. Furthermore, Burgeson et al. does not disclose a method for expressing a fused protein subunit that is designed to trimerize with other expressed fused protein subunits to create a disulfide bond-linked trimeric fusion protein containing more than one (i.e. three) non-collagen polypeptide elements. Accordingly, the claimed invention is clearly not obvious in light of Vuorio et al. and Burgeson et al. since the combination does not teach or suggest every element of the pending claims.

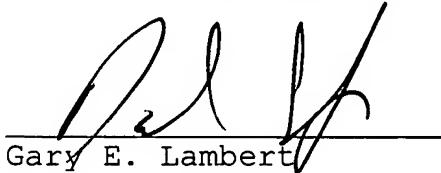
In view of the applicant's amendments to the claims, applicant respectfully requests the Examiner to remove this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to contact them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Amendment. If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account 12-0115.

Respectfully submitted,



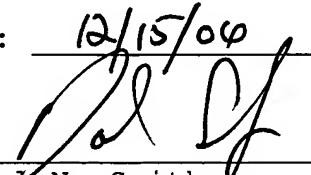
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**CERTIFICATE OF MAILING**

I hereby certify that this Amendment is being deposited with the United States Postal Service in an envelope addressed to the Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 with sufficient first class postage thereon on the date shown below.

Date: 12/15/04  
  
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Daniel N. Smith